Energy flow in growth and production

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Abstract

Growth involves two flows of energy: the chemical energy in the monomers used to construct the macromolecules that comprise tissue (proteins, nucleic acids, lipid membranes), and the metabolic energy used to build those macromolecules. Most ecological models deal explicitly with only the first of these two flows, and some actually confuse them. The metabolic (ATP) cost of synthesising the various macromolecules required to build tissue is well defined, and we have a robust estimate of the overall cost of growth for an individual ectotherm, though not for endotherms (mammals and birds). At the population level the cost of production appears to be much greater for endotherms than ectotherms, the reasons for which are not fully understood (as it involves more than simply their greater resting metabolic rate). These uncertainties are important to resolve if we wish to understand the flow of energy through individual organisms, populations and ecosystems.

Keywords
cost; energy; growth; metabolism; model; thermodynamics

Energy and growth

A key feature of the life-history of any organism is growth, a process that utilises considerable energy. Growth requires raw materials for the assembly of the macromolecules that comprise the bulk of tissue: amino acids for proteins, simple sugars for polysaccharides, purines and pyrimidines for nucleic acids, and fatty acids for the complex lipids of membranes. Energy, in the form of ATP (see Glossary) and GTP, is then used to construct these macromolecules from their precursor monomers. There are thus two flows of energy involved in growth: the chemical energy contained within the monomers, and the metabolic energy used to construct new tissue from them. The former is traditionally estimated from the energy content of the tissue, the latter from oxygen consumption.

A complete understanding of the energetics of growth requires knowledge of both flows. However most of the models of growth to be found in the ecological literature deal explicitly with only one of these two pathways, and a few actually confuse them. In this article I suggest how energy should be handled in models of growth and production so as to conform with what we know of the physiology and thermodynamics of growth, and identify areas for future research.

Metabolism, energy and growth

For most ecologists metabolism is synonymous with oxygen consumption, as this is how it is usually measured. The physiological basis for this is that oxygen acts as the terminal electron acceptor in the regeneration of ATP from ADP (oxidative phosphorylation) and since ATP either directly or indirectly powers pretty much everything an organism does, using oxygen consumption as an estimate of the rate of metabolism is reasonable. This does however involve

two assumptions: firstly that all ATP regeneration involves oxygen, and secondly that all oxygen use is for oxidative phosphorylation. Neither of these assumptions is strictly correct: some ATP can be produced through glycolysis alone, which is anaerobic, and some oxygen is used for other tasks (for example sterol synthesis). The effect of these complications is, however, believed to be small, and the assumption that oxygen consumption is a direct measure of the rate of ATP regeneration, and hence overall metabolic rate, is thus a reasonable one [1].

To fuel its growth the organism must thus supply monomers for synthesis (the anabolic pathway) and substrates for regenerating ATP (the catabolic pathway) (Figure 1). The energy passing along the anabolic pathway is retained in the newly synthesised tissue, the energy passing along the catabolic pathway is almost entirely dissipated as heat. A correct treatment of growth must include both pathways, or the energetics will be wrong.

<Insert Figure 1 about here>

The cost of synthesis

The syntheses of the various macromolecules from which tissue is constructed have important energetic features in common. The peptide bond in proteins, the glycosidic bond in polysaccharides and the phosphodiester bond in nucleic acids and phospholipids are all formed by condensation (dehydration) reactions involving the removal of the elements of water. They all utilise energy from ATP hydrolysis in their formation, and all involve a marked decrease in entropy and an increase in Gibbs (free) energy compared with the free precursor monomers from which they are built.

The formation of a peptide bond between two amino acids requires the hydrolysis of four ATP molecules. Of the roughly 200 kJ mol^{-1} of energy released under typical cellular conditions, only about 8-16 kJ mol^{-1} is incorporated into the bond, with the rest being dissipated as heat. Similarly the formation of a glycosidic bond between two glucose molecules requires the hydrolysis of two ATPs, of which ~17 kJ mol^{-1} is incorporated into the bond. In the formation of phosphodiester bonds again only a small fraction of the energy released from ATP is actually retained in the bond. The bulk of the chemical energy retained in newly synthesised tissue thus comes from the precursor monomers, and only a small fraction comes from the ATP. On the other hand, the bulk of the energy dissipated during macromolecular synthesis comes from ATP (Figure 1).

Despite how it is presented in many textbooks, this dissipation of heat during the synthesis of macromolecules is not inefficiency. After several billion years of selection in an energy-limited world it would be surprising indeed if the core metabolism of organisms were in any way inefficient. Rather it is the dissipation of energy as heat that drives the change in entropy required for the synthesis to be energetically favoured (and is thus a simple consequence of the Second Law of Thermodynamics). The central role of entropy in the energetics of growth has not received much attention by physiologists concerned with growth in vertebrates, but it has long been a central theme in the energetics of bacterial growth [2-4].

The metabolic cost of synthesis can be illustrated by the synthesis of a protein from its component amino acids. Given that the ATP costs per peptide bond are invariant, the metabolic cost per unit mass of protein synthesised, Rs, is:

$$Rs = Cs.P$$

where Rs represents the energy dissipated as heat during synthesis and P the energy retained in the new protein. If P and Rs are expressed in the same units (energy or power), Cs then represents a dimensionless cost of synthesis and the total cost of synthesising unit mass of protein is (P + Cs.P).

Simple calculation shows for the synthesis of a protein of typical amino acid composition [5], Cs = 0.077. In other words, the synthesis of 100 kJ of protein involves the dissipation of ~8 kJ of energy as heat, and the total cost to the organism of producing the nascent polypeptide is 108 kJ. A similar calculation for the synthesis of glycogen from glucose monomers yields Cs = 0.035. These might be termed thermodynamic costs of synthesis, because their basis lies in the dissipation of energy required for the synthesis reactions to be entropically favoured.

The cost of growth

The process of growth involves more than just the synthesis of macromolecules. Within the cell there are also costs to error checking, recycling of mis-folded proteins, post-translational modification of newly synthesised proteins and so on, and the ATP required to provide metabolic energy for synthesis must be moved from the mitochondria where it is regenerated into the cells where it is used. In addition, for complex organisms there are also transport costs: monomers must be mobilised from food or reserves and carried to where they are needed, and these extra costs, over and above those involved with synthesis itself, contribute to the overall cost of growth.

Unlike the cost of synthesis discussed above, the cost of growth cannot be estimated theoretically, for it involves too many process for which the metabolic costs are unknown. It can, however, be estimated empirically. This is done by determining the relationship between the rate of production of new tissue and the rate of metabolism above that required for maintenance. This is shown in the conceptual model in Figure 2a.

<Insert Figure 2 about here>

Using the same approach as for the cost of synthesis (above), we can define a cost of growth, Cg, as:

$$Rg = Cg.P$$

where Rg is the energy dissipated in the synthesis of new tissue P. If we assume that growth costs are additional to maintenance and other routine costs, and again we express both production and metabolism in the same units (energy or power), then the slope of the relationship between Rg and P estimates a dimensionless cost of growth, Cg. Empirical data for a range of ectotherms are shown in Figure 2b, and these yield a value for Cg of ~0.32. The synthesis of 100 kJ of new tissue thus involves the dissipation of 32 kJ of energy as heat, and the total energy the organism must utilise in producing that new tissue is 132 kJ [6]. Ignoring this cost of growth results in a significant error in attempting to balance an energy budget for a growing organism.

In the older literature, the cost of growth is typically expressed as an efficiency, E, where E = 100(1 – Cg). Here E is broadly equivalent to the growth coefficient K3 [7], the net efficiency of growth [8], or the partial growth coefficient [9]. For the evolutionary reasons discussed above, it

is preferable to frame this relationship in terms of costs rather than inverting it to an 'efficiency' (since an 'efficiency' of <100% might imply, wrongly, that growth is somehow not proceeding as effectively as it might be) [6].

In organisms that feed episodically the metabolic costs of growth are seen in the pulse of metabolism that follows a meal. This short-term rise in metabolic rate is still known widely by its original term, the *specific dynamic action* (SDA), but is often also referred to as the *heat increment of feeding* [6] and in the human nutrition field it is also called the *thermic effect of food* or *diet-induced thermogenesis*. It is now clear, principally from work on marine invertebrates, fish, amphibians and snakes, that the SDA is driven by the metabolic costs of processing food, absorption and transport together with the cost of the pulse of growth that follows the meal [10-12]. In many organisms that feed and/or digest almost continuously, such as grazing herbivores, these costs contribute to a general elevation of metabolism rather than the discrete pulse that characterises the SDA.

The costs of synthesis are, as far as we know, invariant. The other costs associated with growth, however, may not be. Indeed there is intriguing evidence that at low cell temperatures a greater fraction of newly-synthesised proteins mis-fold and need to be recycled immediately [13]. This would lead potentially to a variation in the cost of growth with body temperature.

Modelling growth and production

Any model of the flow of energy through organisms must include explicit consideration of growth. In doing so, it must capture both of the flows of energy (Figure 1). Although the two flows of energy involved in growth have been recognised for decades by physiologists concerned with the energetics of domesticated animals [8] they have yet to enter the mainstream thinking of many ecologists concerned with energy flow through organisms or ecosystems.

Furthermore, the two pathways of energy involved in growth are rarely treated explicitly in established ecological models. In the traditional balanced energy budget developed during the International Biological Program, IBP, the energy invested in new tissue is parameterised specifically but the metabolic cost of growth is generally subsumed within an overall respiration term [14]. The respiration term can be partitioned to recognise the cost of growth [15] but is generally only in models of fish energetics that these costs are treated explicitly, usually by identifying SDA as a component distinct from standard metabolic rate and the costs of activity [16, 17].

The next important advance in the modelling of energetics was the development of the dynamic energy budget (DEB) [18]. In the DEB, the energy in new tissue is treated explicitly but although the cost of growth (as SDA) is acknowledged in the thermodynamic rationale underpinning DEB theory, it is again subsumed within general metabolic overheads associated with the production of new somatic or reproductive tissue [19]. These metabolic overheads have to include the costs associated with gaining the necessary resources (foraging, locomotion and so on) as these are not otherwise accounted for in the structure of a DEB model.

The most recent growth model, the ontogenetic growth model (OGM) [20] fails to account for the metabolic cost of growth and assumes explicitly that the energy retained in new tissue is supplied by metabolism. This confuses the two flows of energy involved in growth and contravenes the First Law of Thermodynamics (energy dissipated in metabolism – that is, respiration – cannot also be retained in tissue). Subsequent developments of the OGM

recognised this error [21], and the most recent version, the General Growth Model has a structure essentially identical to the IBP balanced energy budget developed decades previously, though with the addition of a scaling component [22]. Despite these modifications, some recent studies of energy flow through populations continue to assume erroneously that the energy for growth is supplied by metabolism [e.g. 23].

A note on scaling

It has long been known that metabolic rate at rest (usually termed basal metabolic rate in endotherms and standard metabolic rate in fish and other ectotherms), daily energy use and growth all scale with body mass with an exponent of roughly 0.75. A seminal paper provided a mechanistic basis for this scaling in vertebrates [24], by showing that this scaling exponent emerged from the quasi-fractal nature of the circulatory system coupled with the assumption that selection has minimised the energy required for cardiovascular work. Since the cardiovascular system supplies the cells with both nutrients for monomers and oxygen for ATP regeneration, it is not surprising that the scaling of growth reflects this cardiovascular architecture, and also exhibits an exponent of roughly 0.75.

This model forms the core of the Metabolic Theory of Ecology [25] and provides the scaling component of the proposed Universal Growth Model, UGM [20]. The key feature of the UGM is the derivation of dimensionless variables to capture the two components of growth, mass and time. The model matches growth data for vertebrates very well, presumably because it is dictated primarily by the scaling of material and oxygen supply and is insensitive to the error in assigning the energy supply for growth to metabolism. The model is much less successful at capturing growth in invertebrates [26], possibly because many of these have complex life-cycles and also often a very different architecture to their circulatory systems [1].

The cost of production

What happens when we scale up from individuals to populations? Since there is no evidence that the costs of tissue synthesis itself is any different in mammals and birds (endotherms) compared with ectotherms such as fish or insects, we might expect the relationship between respiration and production to be parallel in the two groups when plotted in linear space, but offset because of the greater resting metabolic rate in endotherms (a factor of x 5-10, depending on body mass, when allowance is made for body temperature [1]) (Figure 3a).

<Insert Figure 3 about here>

A relationship between respiration and production in natural communities has long been noted by ecologists. First suggested by Engelmann [27], it has been confirmed by analysis of larger data sets [28, 29]. The distribution of production and respiration data from natural populations is highly skewed and so both variables are typically log-transformed for analyses. In this form the data show a clear linear relationship between respiration and production, with the data for endotherms lying significantly above the data for ectotherms (Figure 3b).

In the original studies [28, 29], the higher cost of production in endotherms (mammals and birds) was related to their higher metabolic rates compared with ectotherms. What has not attracted much attention is that the parallel relationships in log-space indicate a very different cost of production in the two groups, clearly evident when the data are plotted in linear form

(Figure 3c). The data indicate that a population of mammals or birds dissipates considerably more energy per unit of production than does a population of fish or insects (by roughly a factor of 8).

The explanation for this striking difference is far from clear (Box 1). Possibilities include a very different population structures in endotherms and ectotherms, particularly in the proportion of non-growing or reproducing individuals, or differences in the costs associated with foraging and resource acquisition. It has been suggested [30] that the higher power physiology of endotherms has reduced the burden of reproduction, in that the energy content of the offspring form a much smaller proportion of the overall energy budget. An alternative view is that it allows for a more extended period of parental investment (which thus increases the total energy that must be committed to raising young). This is an area ripe for life-history modelling, as long as the basic thermodynamics and physiology are correct.

The different levels of cost

We can thus identify three different levels at which we can see the metabolic costs associated with growth (Table 1). At the molecular level we can quantify the energy dissipated in the construction of macromolecules from their constituent monomers. These costs are of theoretical interest, but exclude many other processes that consume energy, both within the cell and also at the organism level.

<Insert Table 1 about here>

The cost of growth at the organism level is significant, and reasonably well defined empirically (at least for ectotherms). It needs to be incorporated into any model attempting to capture energy flow through an individual organism.

At the population level, the costs of production include may other processes for which we have little knowledge. The costs exceed those well-defined at the organism level by at least an order of magnitude, and differ markedly between endotherms and ectotherms. These costs are poorly understood, but they indicate that quantifying energy flow through communities or ecosystems requires knowledge of population size structure, stage-specific reproductive output, and activity costs. Simply scaling up the energetics of a representative individual to a population or community may well produce misleading answers.

Table 1. Metabolic costs of growth at the cellular, organism and population level

Term	**Definition**	**Dimensionless cost**
Cost of synthesis	Energy dissipated as heat by the cell in the synthesis of a macromolecule from its precursor monomers	0.04 - 0.08
Cost of growth	Energy dissipated as heat by an organism during growth	~ 0.32
Cost of production	Energy dissipated as heat by a population of organisms as a consequence of production	4.0 (ectotherms) 33.8 (endotherms)

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Box 1: Outstanding questions

We currently have an excellent understanding of the ATP costs of synthesising the macromolecules needed for new tissue, and a good empirical measure of the cost of growth at the individual level for ectotherms. There remain, however, several outstanding questions that limit our ability to parameterise growth in ecosystem models.

1. Is the cost of growth for an individual endotherm (mammal or bird) similar to the well-established value for an individual ectotherm? If not, why not?

2. What factors underpin the very much greater costs of production at the population level in endotherms and ectotherms?

3. What are the consequences of these very different costs of production for the way energy flows through communities and ecosystems?

Glossary

ATP. Adenosine-5'-triphosphate. The molecule that delivers the energy released by intermediary metabolism to where it is needed in the cell. Energy is released when ATP is hydrolysed to ADP (adenosine diphosphate) and inorganic phosphate. ATP is regenerated from ADP by oxidative phosphorylation in the mitochondria.

Ectotherm. An organism where the main source of heat is the environment. These are all organisms except mammals and birds.

Endotherm. An animal which maintains a high and relatively stable internal temperature, where the main source of heat is a high metabolic rate at rest. These are mammals and birds; all other organisms are ectotherms.

Entropy. A measure of how energy is distributed within a system. The entropy and temperature together dictate how much of the total energy of a system is unavailable for use (the remaining energy, the Gibbs free energy, being what the system can use to perform work).

GTP. Guanosine-5'-triphosphate. An alternative energy carrier to ATP, important in protein synthesis. It is regenerated from ATP, which allows us to describe the energetics of protein synthesis in terms of ATP turnover alone.

Intermediary metabolism. The suite of reactions that transfers the energy in substrates such as glucose or fatty acids, to ATP. It comprises glycolysis, the tricarboxylic acid cycle (Krebs cycle)

and oxidative phosphorylation. It is termed 'intermediary' metabolism because it lies between the energy stored in reserve substrates and its use in ATP, thereby distinguishing it from all the other reactions that contribute to the total cellular metabolism.

Oxidative phosphorylation. The process of regenerating ATP from ADP and inorganic phosphate, fuelled by the energy released by intermediary metabolism. This energy is carried by electrons and in the final step the electrons are passed to oxygen, which is thereby reduced to water. The rate at which oxygen is used by the organism is thus a measure of the rate of ATP turnover.

Peptide bond. The bond linking amino acid residues together in a polypeptide (protein).

Figure legends

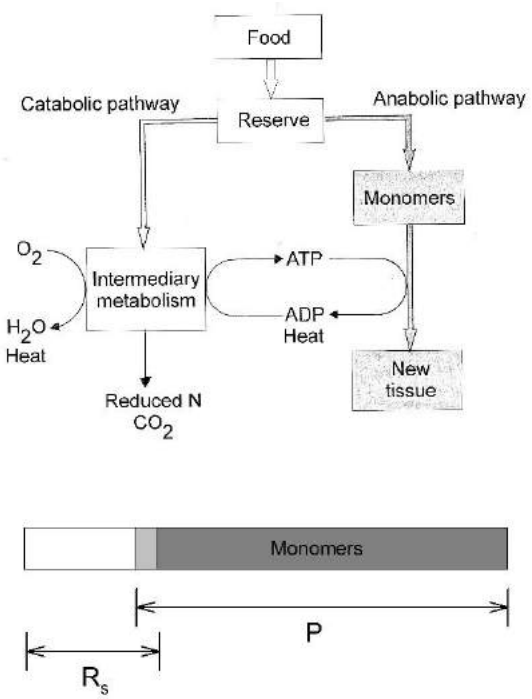

Figure 1. Energy flows in growth. A (upper panel). The two flows of energy involved in growth. The flow of chemical potential energy retained in monomers (the anabolic pathway) is shown in grey, and the catabolic pathway that generates the ATP needed for the synthesis of macromolecules from those monomers is shown in white. B (lower panel). Partitioning of the energy involved in growth. Chemical potential energy in the monomers is shown in grey, the small addition of chemical potential energy shown in light grey (the size has been exaggerated for clarity), and the energy dissipated during synthesis shown in white. P represents the energy measured by bomb calorimetry of the tissue, and Rs the metabolic cost of growth. Note the small element of double counting that follows from the assumption that all of the energy released by ATP hydrolysis is dissipated. Both diagrams modified from [1].

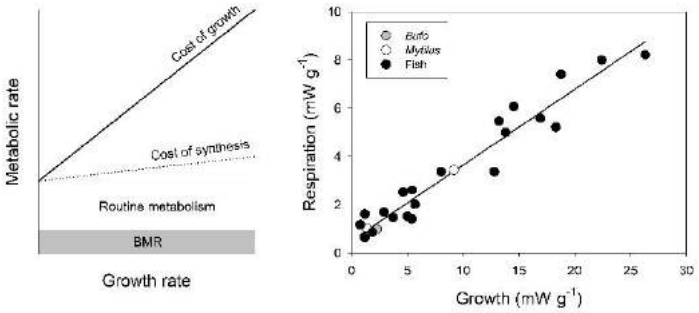

Figure 2. The cost of growth in animals. A (left panel). A conceptual model of the relationship between growth and metabolic rate. This model assumes that the cost of growth is additive (that is, faster growing animals do not reduce either maintenance or routine costs). The cost of synthesis is shown as a dotted line, and the cost of growth as a solid line. B (right panel). An estimate of the cost of growth in selected ectotherms; the slope of the fitted line estimates the dimensionless cost of growth as 0.32. Data from [6].

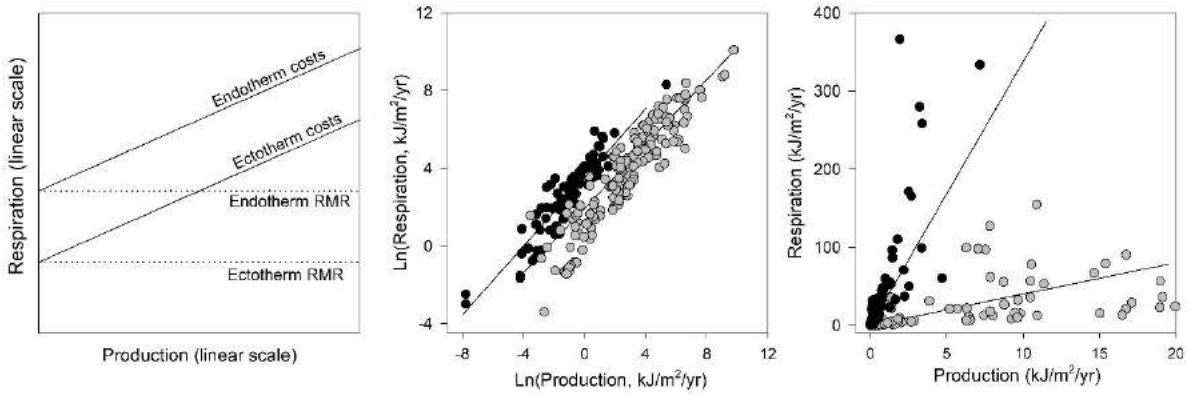

Figure 3. The cost of production in animal populations. A (left panel). Conceptual model of the relationship between respiration and production in populations of endotherms and ectotherms, assuming similar a cost of production in the two groups. RMR: routine metabolic rate. B (middle panel). Relationship between population respiration and population production in free-living populations of endotherms (mammals and birds, black symbols) and ectotherms (predominantly fish and arthropods, grey symbols). Both variables have been transformed (natural logs). The slope of the line fitted by a general linear model (GLM) was 0.88, and the hypothesis that endotherms and ectotherms have identical slopes could not be rejected ($F = 1.59$, $p = 0.21$). Data from [29], but limiting analysis to single-species populations with only a single data point per species. C (right panel). The same data plotted in linear space, showing only the lower values for clarity. The lines represent dimensionless costs of production estimated from the GLM: 4.0 (ectotherms) and 33.8 (endotherms).

Highlights (Required item)
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For almost half a century ecologists have used the balanced energy budget for modelling the flow of energy through organisms and communities.

A recent new model based on the scaling relationship between resting metabolism and body mass has largely replaced earlier models, and is being used increasingly to explore the way energy flows through ecosystems.

This model, and recent applications of it, assume erroneously that the energy for production (growth, reproduction) is supplied by metabolism (in other words, oxygen consumption, for this is how the rate of metabolism is usually quantified).

Understanding how energy flows through biological systems is an increasingly urgent demand given our changing world, but this can only proceed with models that are thermodynamically and physiologically sound.